

Translational Research at NIH

Therapeutics for Rare and Neglected Diseases (TRND)



NIH Center for Translational Therapeutics
National Institutes of Health

November, 2010



Overview

- **What is TRND?**
- **TRND Capabilities & Pilot Projects**
- **What is the TRND Application Process?**
- **Questions**



The Problem of Rare and Neglected Diseases

- ~7,000 diseases affect humankind – but only a small fraction support commercial development of therapeutic agents
- Two types of neglected diseases:
 - Low prevalence, i.e., “rare” (<200,000 prevalence in U.S.)
 - There are >6000 rare (orphan) diseases
 - Cumulative prevalence in U.S. ~ 25 – 30 million
 - Most are single gene diseases
 - <200 have any pharmacotherapy available
 - High prevalence but “neglected”
 - Occur chiefly among impoverished and marginalized populations in developing nations (treatment costs prohibitive)
 - Most are infectious



What is TRND?

- Congressionally-mandated effort to speed development of new drugs for rare and neglected diseases
- Collaboration between intramural and extramural labs with appropriate expertise
 - Solicitation Process
- Projects will:
 - Enter TRND at a variety of stages of development
 - Be taken to phase needed for external organization to adopt for clinical development





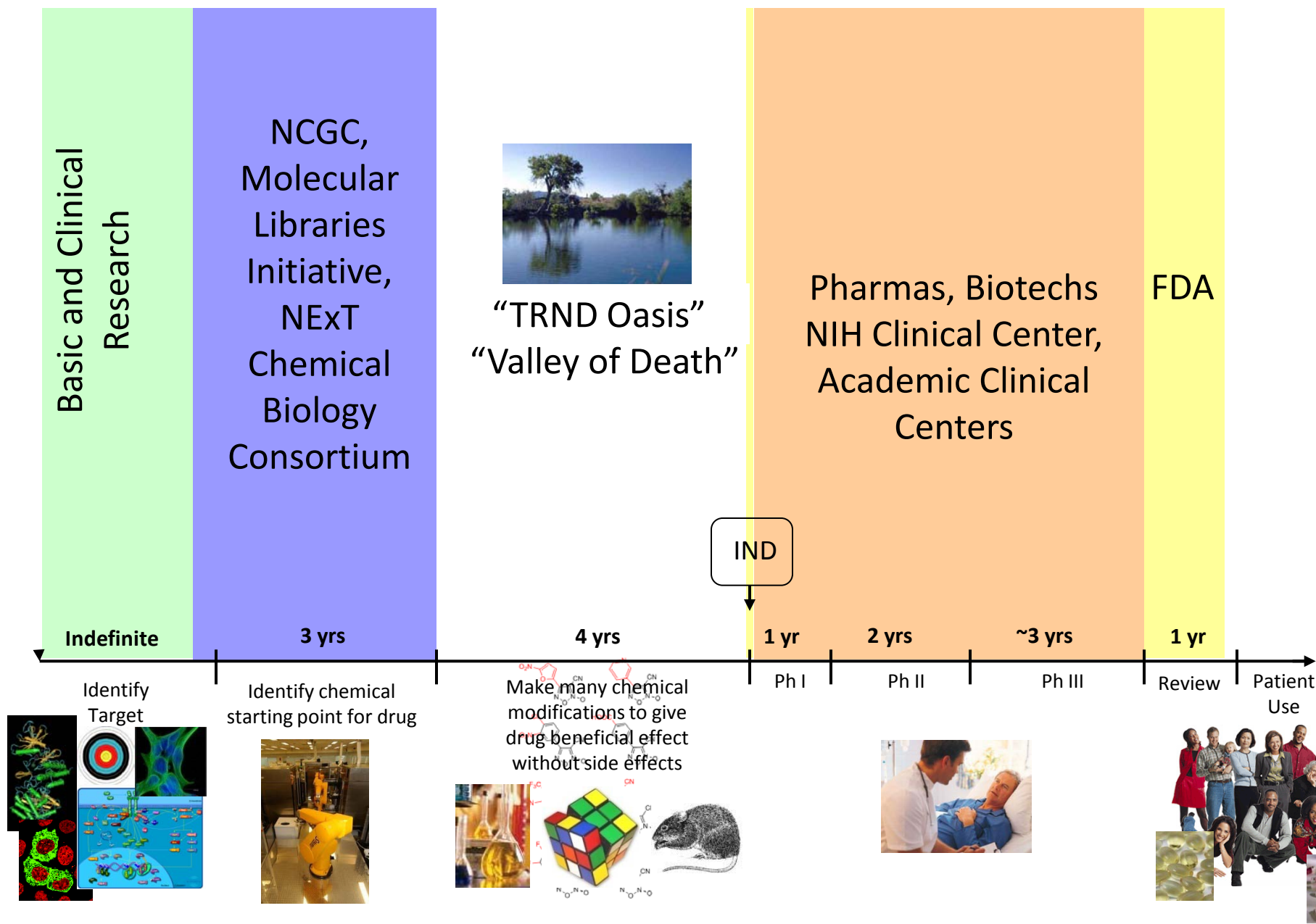
TRND

Creating a Drug Development Pipeline at NIH

- **Drug Development Intramural Laboratory with External Disease and Target Collaborators**
 - Government, Academics, Non-Profit, For-Profit collaborations
- **Distinguishing features**
 - Collaboration / Partnerships (not service center)
 - Building the laboratory and expertise infrastructure at NIH
 - Disease agnostic, take advantage of cross-cutting mechanisms
 - *Science* of preclinical drug development
 - Technology/paradigm development (20% of effort, toward improving success rates)
 - Large-scale systematic repurposing
- **Project-specific activities**
 - Medicinal chemistry
 - Efficacy, pharmacology, ADME, toxicology, PK/PD
 - Compound scale-up, formulation
 - First in human clinical trials as needed for project



The long pathway to drug development





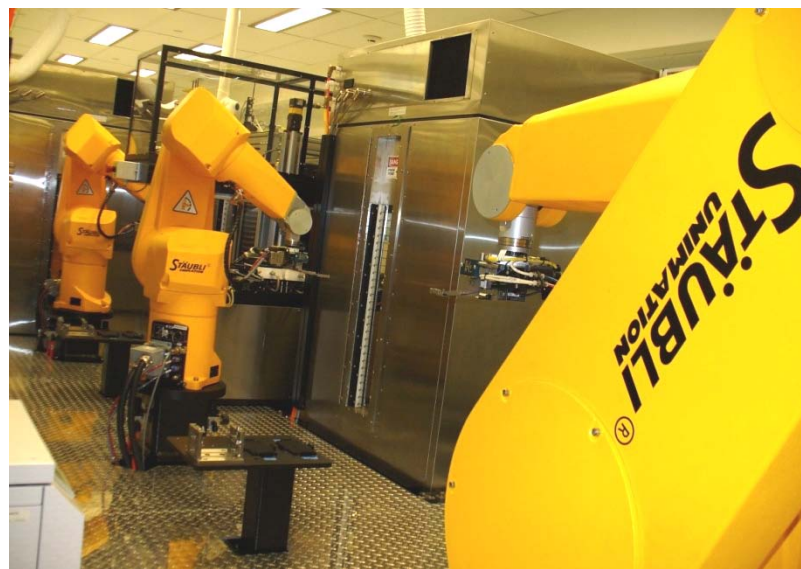
TRND Program Timeline

- FY09: infrastructure (May 2009)
- FY10: infrastructure and pilot projects (June 2010)
 - Budget \$24M
 - Focus: governance, hiring, research community outreach, pilot projects
- **FY11: infrastructure and project solicitation**
 - **President's budget recommends \$50M**
 - **Solicitation of projects in Sept 2010 to begin in April 2011; 3-5 projects**
- FY12: fully operational
 - Laboratories (40,000 sq ft) completed December 2011
 - Work on several new projects per year
 - Average project should take ~3 years
 - Projects will be monitored closely for progress

TRND Builds on a Foundation of Success

NIH Chemical Genomics Center

- Founded as part of Roadmap
- 75 scientists
- > 100 collaborations with investigators worldwide
 - 75% NIH extramural
 - 15% Foundations, Research Consortia, Pharma/Biotech
 - 10% NIH intramural
- Focus on novel targets, rare/neglected diseases
- Produces
 - chemical probes/leads
 - new paradigms for assay development, screening, informatics, chemistry



Rare/neglected disease projects at NCGC

- Ataxia-telangiectasia
- Beta-thalassemia
- Charcot-Marie-Tooth
- Chordoma
- Chronic lymphocytic leukemia
- Gaucher disease
- Huntington's disease
- Leishmaniasis
- Lymphangiomyomatosis
- Malaria
- Myotonic dystrophy
- Niemann-Pick C
- Progeria
- Retinitis pigmentosa
- Schistosomiasis
- Spinal muscular atrophy
- Trypanosomiasis

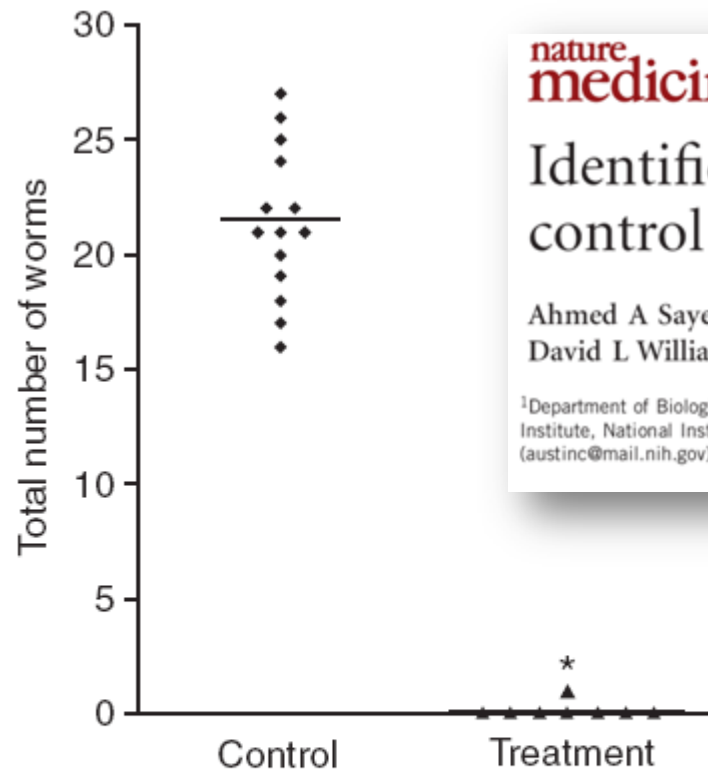
Developing a new drug for schistosomiasis



- Parasitic disease that affects 250 million people, mostly in Africa
- Currently controlled by praziquantel (PZQ)
 - Cure rates not 100%
 - Evidence that schistosomes could become resistant to PZQ → search for new treatment options
- NIH grantee Dr. David Williams
 - Identified potential new target
 - Collaborated with NCGC to develop new lead series



Developing a new drug for schistosomiasis



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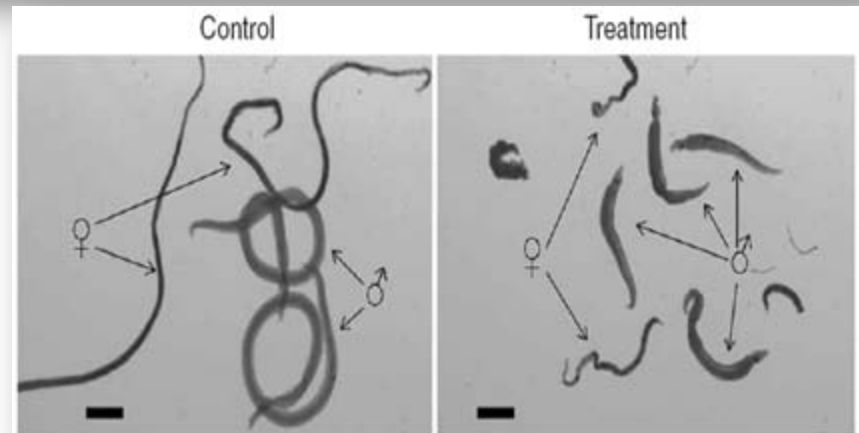
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Identification of oxadiazoles as new drug leads for the control of schistosomiasis

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TRND Pilot Projects

Chosen to establish processes in advance of solicitation, with diversity of project stage, type of disease and collaborators

Disease	Type	Pathology	Collaborators	Compound type	Stage
Schistosomiasis, Hookworm	Neglected	Infectious parasite	Extramural	NME	Lead optimization
Niemann Pick C	Rare	CNS, liver/spleen	Disease Fnd, Extramural, Intramural	Repurposed approved drug	Preclinical Development
Hereditary Inclusion Body Myopathy	Rare	Muscle	Biotech, Intramural	Intermediate replacement	IND-enabling studies
Sickle Cell Disease	Rare	Blood	Intramural, Biotech	NME	IND-enabling studies & clinical trials design
Chronic Lymphocytic Leukemia	Rare	Cancer	Disease Fnd, Extramural	Repurposed approved drug	Pre-IND

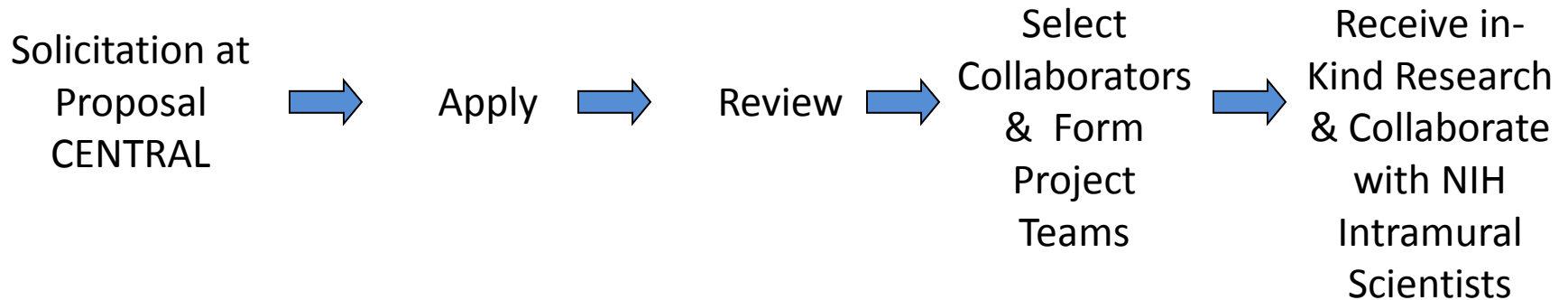
How to apply to TRND

TRND is Different

Usual NIH mechanism



TRND



http://trnd.nih.gov



THERAPEUTICS FOR RARE & NEGLECTED DISEASES

Bridging the Gaps in Discovery and Development of Therapeutics for Rare and Neglected Diseases

Posts Comments

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Home

The **National Institutes of Health** (NIH) Therapeutics for Rare and Neglected Diseases program is a congressionally mandated program to encourage and speed the development of new drugs for rare and neglected diseases. This unique program creates a center within the NIH and is specifically intended to stimulate research collaboration between scientists, non-profit organizations, and pharmaceutical and biotechnology companies to address rare and neglected illnesses.

The TRND program provides an opportunity to partner with, and gain access to, the scientific capabilities, expertise, and resources in a collaborative environment to bring promising therapeutics into clinical testing. TRND will use an application review process to select collaborators. If the application is successful, the applicant(s) will partner with TRND to advance a drug development program. TRND investigators will provide scientific and operations, and the applicant investigator(s) will provide starting materials and ongoing biological/disease expertise throughout the project.

General Instructions

At this time, TRND is considering only **small molecule or biologic therapeutic development projects** for collaboration. Devices, diagnostics, and medical procedures are not responsive at this time.

Proposed projects must target an untreated or poorly treated rare or neglected disease, as defined here:

- http://rarediseases.info.nih.gov/files/Rare_Diseases_FAQs.pdf
- http://rarediseases.info.nih.gov/files/Neglected_Diseases_FAQs.pdf.

Special consideration will be given to projects with the potential to address more than one rare or neglected disease by virtue of shared pathophysiology, and projects with a well-developed strategy to exit TRND and complete clinical development, registration, and marketing.

Projects must be at least at the stage of a validated lead series in order to be considered for TRND. Projects requiring earlier-stage resources, including assay development, high-throughput screening, and initial medicinal chemistry optimization of screening hits, are not appropriate for TRND; researchers interested in these resources are directed to other NIH resources including the **Molecular Libraries Program** and the **NCI Chemical Biology Consortium/NEXT program**.

This "TRND Concept Application" includes six (6) sections as described in detail below; additional material can be uploaded as an appendix. Please use the TRND Concept Application Template, available only when the solicitation is open, at **proposalCENTRAL**. Please convert all documents to searchable PDF files before submission. All materials submitted to proposalCENTRAL are considered confidential. All reviewers will sign conflict of interest and confidentiality agreements before being given access to applications.

TRND encourages potential applicants to contact TRND staff via our webpage at http://trnd.nih.gov/?page_id=121 prior to submitting a proposal in response to this solicitation.

Required Documents for Therapeutics for Rare and Neglected Diseases Program Applications

A. TRND Concept Application

The concept application document should not exceed 5 pages (Arial 11pt, single space, 1" margins). Graphs, pictures and tables should be included in the text. The application should succinctly define the scientific nature and rationale of the proposed project and the current stage of its development, and should include the following:

Application

Timeline, milestones, and key milestones points based on the evaluation recommendations.

B. Appendices

- **References:** Please provide no more than 15 references that relate directly to the project.
- **Public Abstract:** The selected drug development projects that put collaborative agreements into place with TRND will have a public abstract and timeline posted on the TRND website. Please provide a non-confidential abstract that describes the disease, the projects, the medical treatment goals, and the timeline.
- **Intellectual Property (IP) Information:** The applicant should include a list of any patents issued or pending with respect to either the agent or to any non-commercially available technology/material required for the development of the agent. In the event that an application requires the use of non-commercially available technology/equipment that is patented by a third party, the applicant must provide documentation that the patent holder does not object to the applicant's use with the proposed project.

Each TRND application must include the information described below signed by an authorized staff member overseeing IP and/or technology transfer at the applicant's institution or company. This verifies that he/she has reviewed the TRND request and that the technology is eligible for consideration by the TRND program. If the technology is found not to be eligible for use as outlined in the TRND application, and it is central to the investigator's proposal, submission to the TRND program is not encouraged.

If available, the following information is requested:

- Details of all the following rights that are owned by your institution and will be used in the project (the "institution's IP"):
 - Patents and patent applications
 - Significant know-how
 - Registered trademarks, applications for registered trademarks, and other marks
 - Registered designs, applications for registered designs, and significant other designs
 - Significant copyright works and other IP rights
- Details of all employees, consultants, and other parties involved in the development of the institution's IP related to the TRND project submission. (Are there contributors outside the institution, and if so, what was their role in development?)
- A complete list and brief description of all agreements with third parties related to the TRND project submission:
 - Granting rights to those third parties under the institution's IP
 - Granting rights under third-party IP to the institution
- A complete list and brief description of all confidentiality agreements with third parties related to the TRND project proposal
- Details of any:
 - Claims made by third parties against the institution related to the project proposal that the institution has infringed a third party's IP rights
 - Circumstances where a third party has or may have infringed the institution's IP or other IP used in the institutions' business related to the project proposal

Institution IP constitutes background IP. Invention of new IP created from this partnership/collaboration will be determined according to patent law.

- **Key Investigators Biosketch:** All Key Investigator (all investigators intellectually involved in the project) bio-sketches should follow the NIH standard format (<http://grants.nih.gov/grants/funding/phs398/phs398.html>). In the list of publications, please highlight any that are directly related to proposed project by preceding them with a double asterisk



HOME ABOUT TRND RESOURCES APPLY TO TRND

TRND Program Application

Overview

This is not a grant application. Rather, it is a request for TRND, with the goal of moving promising drug development projects to TRND to develop and execute a milestone program. The applicant collaborator(s) must be appropriate and with the support of TRND.

As discussed above, the primary focus of TRND is on neglected disease. It is expected that projects of well-characterized disease with clear endpoints and well-defined endpoints will be required, with well-defined endpoints.

The purpose of this collaborative solicitation is to identify and support drug development projects that are well-suited for TRND.

Required Documents for Program Application

A. TRND Concept Application

The concept application should be included in the application and the current stage of the project.

1. **Background:** Provide a brief description of the disease or biologic therapeutic agent, describe the competitive landscape, and describe the competitive landscape.
2. **Therapeutic Hypothesis:** Provide a brief description of the disease, the therapeutic hypothesis, and the evidence that validates the hypothesis.
3. **Current State of Project:** Provide a brief description of the current state of the project, including the structure-activity relationship (SAR) model, the high-quality New Drug Application (NDA) studies demonstrating the efficacy and safety of the drug, and the formulation studies.

1. Background

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THERAPEUTICS FOR
RARE & NEGLECTED
DISEASES

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Grant Opportunities - Deadlines displayed in **U.S. Eastern Time**

NIH - Therapeutics for Rare and Neglected Diseases

If you would like to check for a specific grant making organization, you may utilize the drop-down list above. To see all available opportunities, select "Show All"

Grant Maker	Programs (Click for Guidelines)	LOI Deadline	Proposal Deadline	Contact Information	FAQ
NIH - Therapeutics for Rare and Neglected Diseases	NIH - Therapeutics for Rare and Neglected Diseases		12/6/2010 5:00:00 PM	-	

Session Timeout: To avoid loss of data, we recommend that you save your work every 10 to 15 minutes. For security reasons, if your session is idle (i.e. if you don't press Save or click on a link to go to another page) within 60 minutes, you will be automatically logged off. Any unsaved data will be lost.

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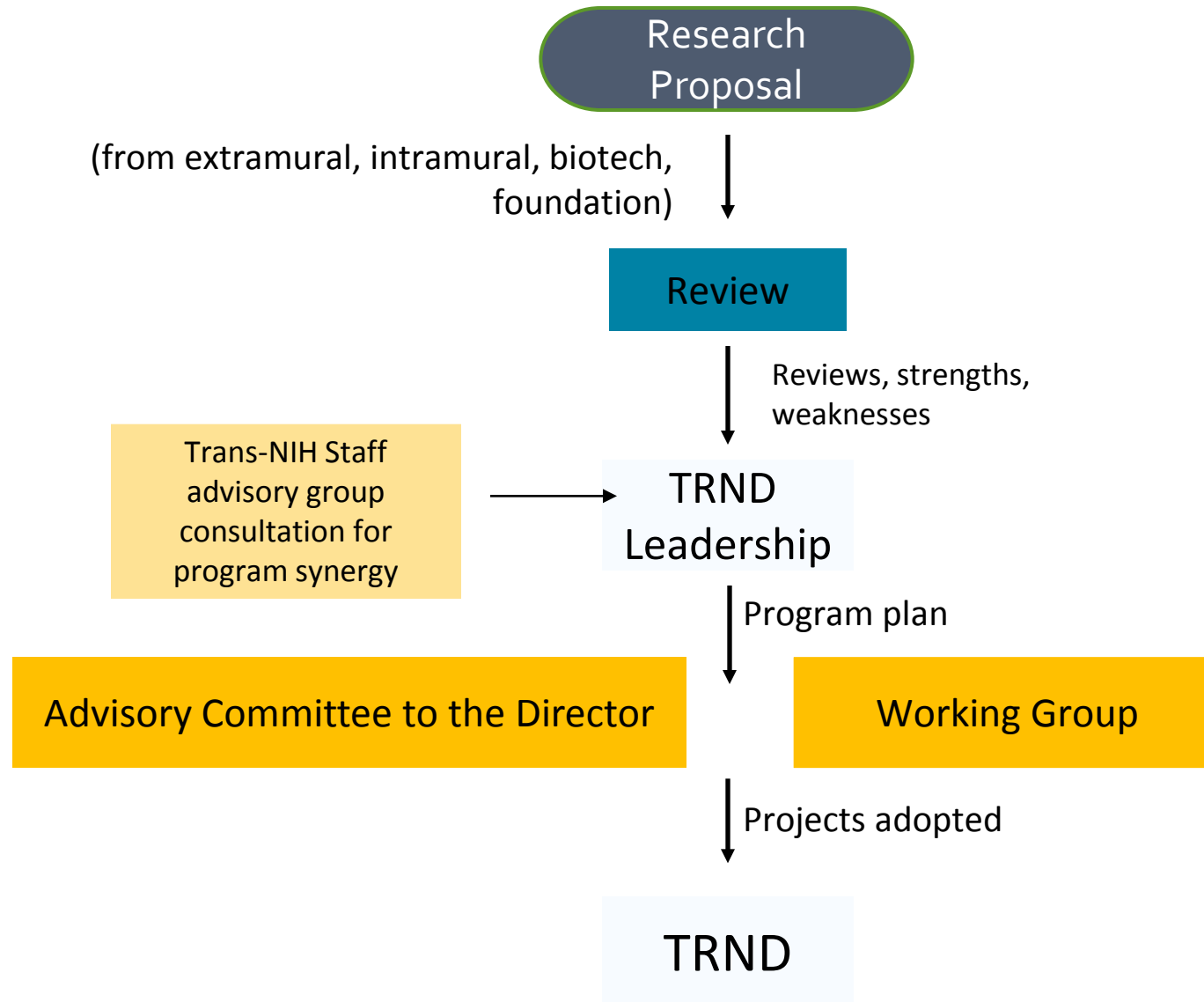
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<https://proposalcentral.altum.com/default.asp?GMID=80>

TRND Project Selection

TRND: Project Selection



TRND Program Evaluation Criteria (criteria and weight of criteria):

- Target and therapeutic validation (30%)
- Strength of current data package (30%)
- Feasibility to reach First in Human (20%)
- Medical impact relative to current Standard of Care (10%)
- Likelihood of external adoption (10%)



TRND Program Evaluation Criteria

rate the strength of the development project

- Medicinal Chemistry
- ADME
- PK/PD
- Toxicology
- In vivo models
- Secondary and tertiary assays
- Formulation
- Chemical Manufacturing and Controls (CMC) – small molecules
- Expression/Purification – Biologics



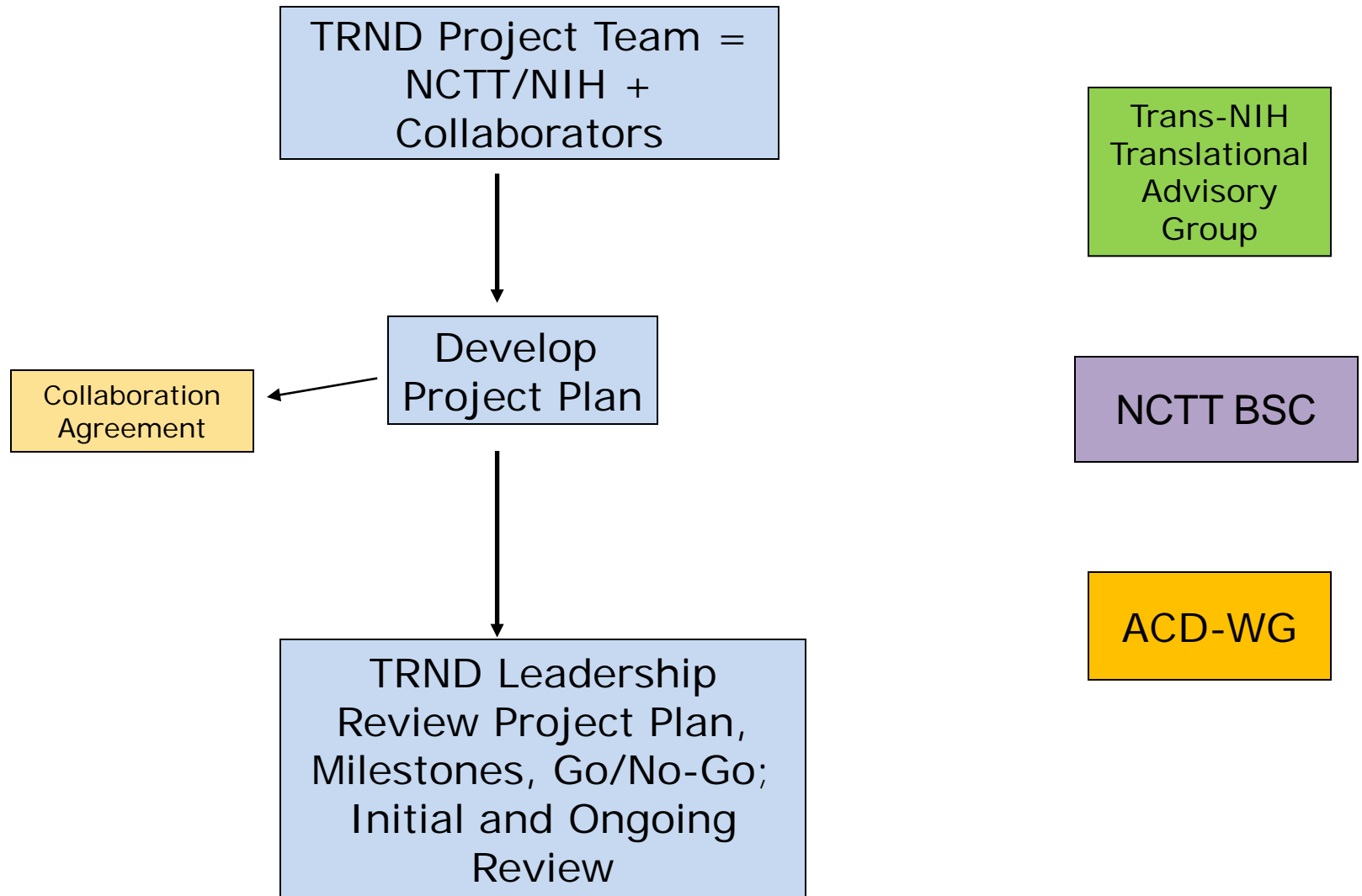
Rare Disease Research Programs

Program success increases with:

- Animal models to establish efficacy
- Clinical translation, establish clinical endpoints
- Patient population well defined with registries
- Biobanks
- Natural history studies complete
- Market opportunity analysis



TRND: Project Management

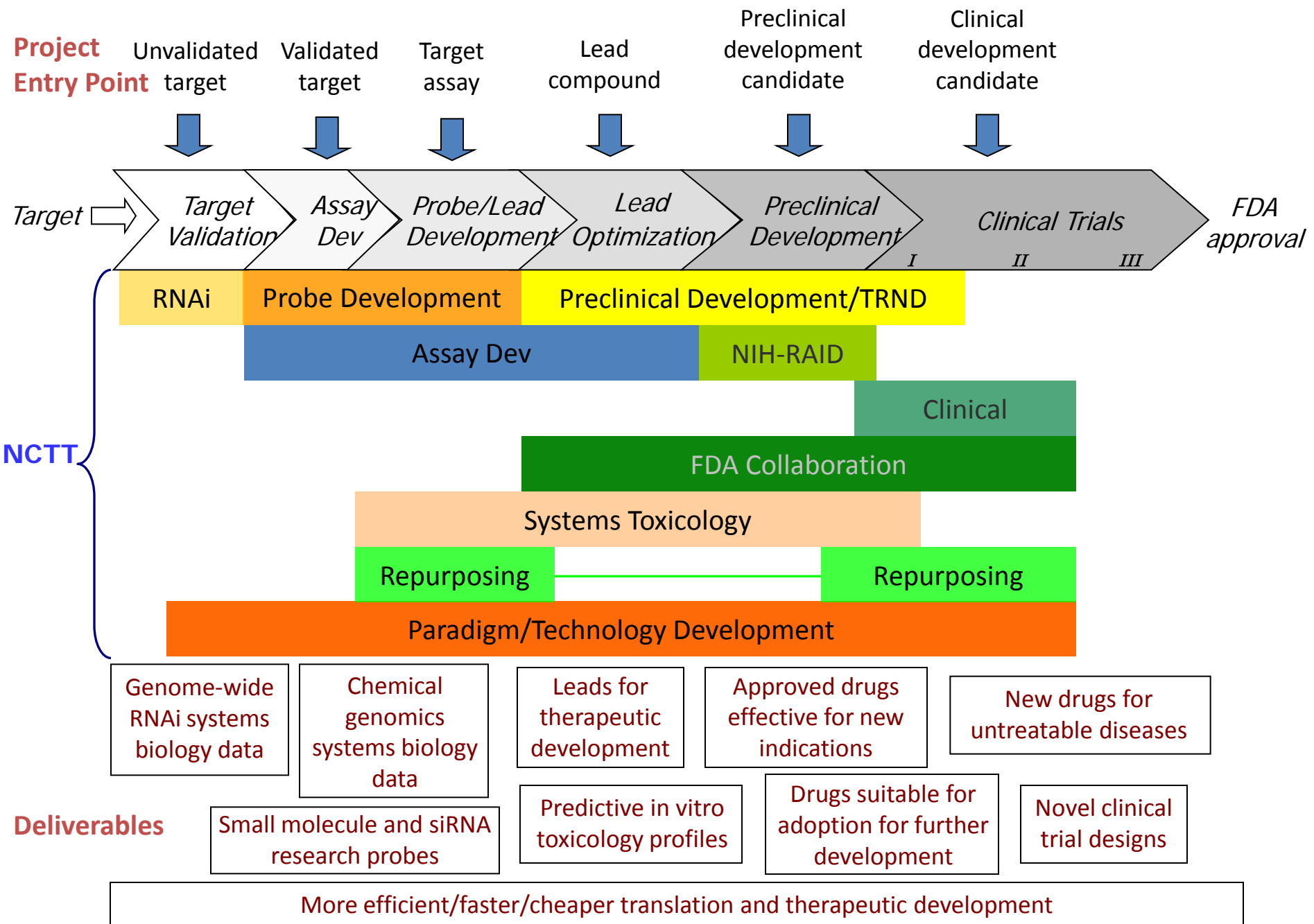


IP

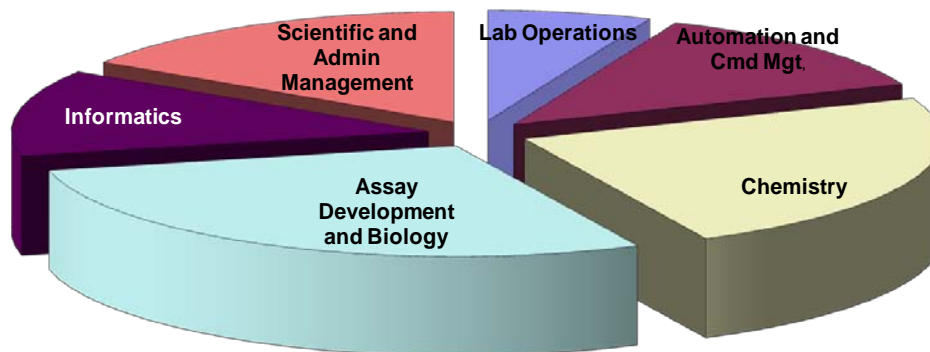
- Institution IP constitutes background IP.
- Inventorship of new IP created from this partnership/collaboration will be determined according to patent law.



NIH Center for Translational Therapeutics: An Integrated Pipeline



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Further Information



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TRND.nih.gov